

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/JP2005/000811

International filing date (day/month/year)
18.01.2005

Priority date (day/month/year)
23.01.2004

International Patent Classification (IPC) or both national classification and IPC
G01N33/543, G01N33/52

Applicant
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1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/JP2005/000811

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/JP2005/000811

Box No. V Reasoned statement under Rule 43*b*/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	7-11
	No: Claims	1-6
Inventive step (IS)	Yes: Claims	None
	No: Claims	1-11
Industrial applicability (IA)	Yes: Claims	1-11
	No: Claims	None

2. Citations and explanations

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

Reference is made to the following documents:

D1: WO0107653

D2: WO9917119

D3: Lab on a Chip, 2001, 1, 153-157

D4: Analytical Sciences, 19, 2003, 15-22

D5: Pure Appl. Chem., 74, 2002, 2299-2309

D6: Anal. Chem., 74, 2002, 379-385

D7: Anal. Chem., 75, 2003, 1116-1122

Attention is drawn in particular to all passages of these documents as indicated on the International Search Report, unless stated otherwise.

1. Subject matter of the application

The present application is predicated on the use of the known laminal flow technique for the detection of substances in a fluid sample under analysis. In the phenomenon of laminal flow of liquids, the dimensions of channels located in a device (here, the 'detecting element' of claim 1 of the present application) are chosen such that when a fluid sample is applied to such a channel, the liquid under analysis will flow therein as a plurality of 'layers' ('lamina'). In the present application, in exploiting the fact that the fluid sample applied to such channel ('microchannel') may be considered to flow as a plurality of essentially independent fluid layers, a plurality of 'detecting means' (the 'substance trapping portions' of claim 1) are located in the channel in such a way that a plurality of substances in the fluid sample may be analysed / detected within a single (microfluidics) device.

Claim 1:

A detecting element, having a) a channel able to form a plurality of layers of flow of a liquid [ie of appropriate dimensions such that liquids applied thereto flow in a laminar fashion - eg page 12 of application, dimensions of 100µm width and 100µm depth], b) a plurality of 'substance trapping portions' in the channel, c) said elements b) being separated and

arranged to independently acquire information on each of the substances in the sample being analysed.

Fig. 2 of the application shows how such elements of a microfluidic device may be envisaged, especially with respect to the relation between the microchannel and detecting elements.

Claim 7:

Effectively the means of the present application for using the device recited in claim 1.

Other claims:

Specification of various preferred embodiments of the device / the use thereof, eg with respect to the substance trapping portions of the device, such have antibody immobilised thereon [the antibody for example binding to an analyte present in the fluid sample under analysis].

2. Prior Art.

D1: Microchannel based device / means for detecting different analytes in a sample after their binding to their cognate binding partners. Such binding partners are immobilised in different sections of the microchannel. In use, sample is passed down the microchannel, target analyte retained, the remainder of sample eluted; thereafter, bound analyte is released and detected / measured. The microchannel preferably has two or more immobilised binding partners specific for two or more analytes to be analysed, located in different regions of the microchannel; upon release of two or more analytes from two or more binding partners, segregation of analytes remains, and the analytes can be separately detected. See D1, page 2, line 20 -page 4, line 21.

D2: Microfluidic devices in detection of analytes. Makes reference to various techniques which can be used in detection means (eg fluorescence, chemiluminescence).

D3: ELISA on a microchip

Other prior art, D4-D6: Microfluidic systems, see comments hereinafter; **D7:** protein chip with antibodies for detection, see comments hereinafter.

3. Novelty (Art. 33(2) PCT)

- In light of D1, the subject matter of claims 1, 2, 6 (D1, page 2, lines 23, 24, binding partner for binding analytes can be an antibody) clearly lacks novelty.

- At present the subject matter of claim 7 is unclear, since the nature of the technical feature apparently sought to be specified by the phrase beginning 'switching and passing ...' is unclear. In order to be able to give an opinion on novelty and inventive step of the subject matter of this claim, interpretation has been made that this phrase reads 'thereafter passing through the channel in which the plurality of different substances have been trapped a fluid which enables the acquisition of independent information on each of the substances in the specimen through an action between the fluid and the trapped substance'. In D1, analytes in a sample which have been previously bound (trapped) in the microchannel are released and flushed past a detector (D1, page 2, lines 29, 30), the spatial segregation of the released analytes being maintained (D1, page 3, lines 10-12). Over D1, the subject matter of claim 7, and claims 8-11 dependent thereon, thus appears to be novel.

- Claims 3-5 specify (recite) technical features of the specimen (sample) to be used in (ie passed through) the detecting element of claim 1, and as such do not specify any further technical features of the device being claimed in claim 1. Accordingly, the subject matter of these claims also lacks novelty in light of D1.

4. Inventive Step (Art. 33(3) PCT)

Whilst possibly novel, the subject matter of claim 7 lacks inventive step for the following reasons. The acquisition of information on a substance trapped or otherwise present in a microfluidic channel by passing a fluid over or in the neighbourhood of the substance, and wherein the fluid comprises an element interacting with the substance to produce a detectable signal indicative of the presence of the substance would appear routine in the art. As an example of this technique, see for example D2, page 2, line 2 - page 3, line 6; examples on pages 19, 20, figures 1 and 10, and D3, page 154, paragraphs 1-3, figure 1. Accordingly, the subject matter of claim 7, and in addition that of claims 8-11 lacks inventive step (the additional features recited in claims 8-11 also appearing to be features which would be derived as a matter of routine practice in the field concerned).

5. Other comments

There would appear no other subject matter in the application as filed which is both novel and inventive. In this respect, the following comments should be noted.

5.1 Use of each of the enzymes listed in claim 5 in the detection of entities in assays (eg immunoassays) is routine in the art. See eg D6, page 384, figure 7; D7, page 1116, paragraph 2 - page 1119, paragraph 1. The latter document also details antibody based detection methods for human AFP and human β 2-microglobulin using antibodies to these entities as 'capture antibodies (D7, page 1117, bottom of left hand column); the examples of the present application are concerned with the capture and detection of exactly the same entities.

5.2 Concerning the preferred microchannel devices of the present application as schematically drawn in figures 1/3 and 7:

these devices have a microchannel arrangement ('principle microchannel') such as of the nature disclosed in D1 and as discussed hereinabove, 'substance trapping portions' arranged in said microchannel as per D1, and the additional features as compared to D1 of having two (fig. 1/3) or three (fig. 7) microchannel branches 'preceding' the 'principle microchannel'. Such arrangement of microchannels whilst apparently novel over D1 is broadly known from other items of prior art: see for example D4, page 17, figure 4; D5, page 2302, figure 3, page 2303, figure 5, page 2306, figure 8; D6, page 383, figure 5.